

REMARKS

Status of the Claims

Claims 1-27 are pending. Claims 17, 20-21 and 25-27 are amended herein. Claims 1-16 are withdrawn from consideration. Applicants respectfully submit that no new matter has been added.

Rejection under 35 U.S.C. § 103(a)

Claims 17-27 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Matsumoto *et al.* (2001) "Structure-Activity Relationship of Ghrelin: Pharmacological Study of Ghrelin Peptides." Biochemical and Biophysical Research Communications 287: 142-146 ("Matsumoto") in view of U.S. Patent No. 6,967,237 ("the '237 patent"), and further in view of Voet and Voet (1995) Biochemistry (2nd Ed.) 60-62, 77 ("Voet").

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *See* Manual of Patent Examining Procedure, 8th Ed., Rev. No. 5 at §§ 2142-2143.

Claim 17 is directed a method for preventing degradation of a hydrophobic group of ghrelin or its derivative in a solution comprising the ghrelin or its derivative comprising adjusting the pH of the solution in the range of from 2 to 7.

The Office Action cites to Matsumoto to demonstrate that charge has an effect on ghrelin activity. The Office Action concedes that Matsumoto does not teach the use of acetic acid as a buffer, nor "does it explicitly mention the pH of the solution." *See* O.A. at 4. The Office Action cites to the '237 patent to show that ghrelin analogs can be prepared as acidic or basic salts. Finally, the Office Action cites Voet for the general proposition that amino acids such as glycine are protonated at low pH values.

The cited references alone, or in combination, fail to teach or suggest every claim limitation. Indeed, the references do not teach or suggest adjusting the pH of the solution comprising ghrelin or its derivative in the range of from 2 to 7, let alone adjusting the pH of this

solution to prevent degradation of a hydrophobic group of the ghrelin or its derivative. The references also fail to teach or suggest the limitations in each of the dependent claims. For example, the references do not teach or suggest that the concentration of the pH adjuster or the buffer agent is in the range of 0.01 mM to 1000 mM.

The Office Action asserts that it would have been obvious to modify Matsumoto because the '237 patent and Voet teach that a positive charge in a ghrelin molecule is maintained by converting the ghrelin molecule to an acid salt. The Office Action further states that the "motivation for maintaining the pH in the range of 2-7 stems from the fact that the ghrelin, and ghrelin derivatives show higher activity when it is positively charged as taught by Matsumoto." See O.A. at 5.

Initially, Applicants respectfully submit that neither the '237 patent nor Voet teach or suggest a positive charge in a ghrelin molecule is maintained by converting the ghrelin molecule to an acid salt. Furthermore, the Office Action has not shown where in the references the "motivation for maintaining the pH in the range of 2-7" is found. Indeed, neither the '237 patent nor Voet provide any suggestion or motivation to modify Matsumoto by adjusting the pH of a solution for any reason, and in particular, to prevent degradation of a hydrophobic group of ghrelin or its derivative.

The Office Action concludes that there would have been reasonable expectation of success "given the knowledge that protonated ghrelin molecules would have higher activity combined with the hydrophobicity at the 3rd residue at the N-terminal end." See O.A. at 5. The Office Action, however, does not provide any evidence to support this statement.

In view of the above remarks, Applicants respectfully submit that the Office Action has not established a *prima facie* case of obviousness. Accordingly, Applicants respectfully request withdrawal of the obviousness rejection.

CONCLUSION

Applicants respectfully submit that claims 17-27 are in condition for allowance, and such disposition is earnestly solicited. Applicants also respectfully request rejoinder and allowance of all pending claims 1-27. Should the Examiner believe that any issues remain after consideration of this response, the Examiner is invited to contact the Applicants' undersigned representative to discuss and resolve such issues.

It is believed that no fees are required for entry of this response, but should any fees be necessary, the Commissioner is authorized to charge such fees to the undersigned's **Deposit Account No. 50-0206**.

Respectfully submitted,

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